

Amendments to the Specification:

Please replace the paragraph beginning at page 27, line 4, which starts with "The IRES from encephalomyocarditis virus" with the following paragraph:

The IRES from encephalomyocarditis virus (EMCV) is available as a 600 bp EcoRI-NcoI fragment, where the NcoI site (CCATGG (SEQ ID NO. 1)) defines the start site of translation; it also contains a HindIII site introduced some nucleotides upstream of the NcoI site, changing the spacing between the IRES and the ATG (Ghattas et al., Mol. Cell. Biol. 11, 5848-5859, 1991). First, the upstream EcoRI site is converted, by linker insertion (sequence AATTGATATCAATT (SEQ ID NO. 2)) to an EcoRV site. Two versions of the IRES are employed, one (IRES-1) in which the heterologous coding sequence is introduced at the NcoI site, a second in which site-directed mutagenesis is used to position the ATG within the NcoI site 20 nucleotides downstream of box A (TTTCC (SEQ ID NO. 3), Pilipenko et al., Cell 68, 119-131, 1992), removing the HindIII site (the DNA sequence in this region now reading TTCCTTTGAAAAACACGATAACCATGG (SEQ ID NO. 4)) (Fig. 13, A). The modified IRES is termed IRES-2. IRES-1 and IRES-2 are both used, as EcoRI-NcoI fragments, for the following experiments.

Please replace the paragraph beginning at page 27, line 31, which starts with "Immediately downstream of the translation stop codon" with the following paragraph:

Immediately downstream of the translation stop codon in the last exon lies a unique AatII site (GACGT/C (SEQ ID NO. 5/SEQ ID NO. 6)). This site is converted, by insertion of a linker, to an EcoRV site (final sequence GACGTGATATCACGTC (SEQ ID NO. 7)) (Fig. 13, D). Although this construction is based on the use of the entire Sall-Sall fragment, the Sall-XbaI fragment may also be used with appropriate minor modifications to the procedure.

Please replace the paragraph beginning at page 28, line 1, which starts with "The reporter gene used in this experiment is human alpha-1 antitrypsin cDNA" with the following paragraph:

The reporter gene used in this experiment is human alpha-1 antitrypsin cDNA though the procedure can be repeated with any other cDNA. The cDNA is engineered, by localised mutagenesis, such that an NcoI site overlaps the initiating ATG (this may lead to a single base change in the second codon, so changing the nature of the amino acid encoded at this position. Because in most cases this amino acid does not contribute to the mature protein because it is at the beginning of the signal sequence this has no adverse consequences for expression, secretion or activity of the mature protein). Similarly, an EcoRV site is engineered at the 3' terminus of the cDNA such that the 3' untranslated region is removed (sequence at the 3' terminus of the cDNA reading TAAGATATC (SEQ ID NO. 8), where the stop codon TAA could be TAA, TAG or TGA) (Fig. 13, B). The NcoI-EcoRV fragment (obtained, where necessary, by partial digestion in cases where internal sites are present) is used in the following experiments.

Please replace the paragraph beginning at page 28, line 19, which starts with "Next, pPolyIII-I (Lathe et al., Gene 57, 193-201, 1987) is modified such that a synthetic" with the following paragraph:

Next, pPolyIII-I (Lathe et al., Gene 57, 193-201, 1987) is modified such that a synthetic BamHI-SaII-PstI polylinker is inserted between the BamHI and PstI sites (sequence of polylinker – GGATCCGCGTCGACCACTGCAG (SEQ ID NO. 9); restriction sites are underlined) (Fig. 13, C). The SaII-SaII fragment encompassing the modified (EcoRV site at the place of the AatII site) genomic ovine BLG gene is cloned into the SaII site. The IRES and the modified cDNA are excised as EcoRV-NcoI and NcoI-EcoRV fragments respectively, ligated together, and the fusion product EcoRV-NcoI-EcoRV inserted into the EcoRV site within 3' untranslated region of the BLG gene (Fig. 13, E).